

CORRECTED VERSION

## PATENT COOPERATION TREATY

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CORRECTED VERSION

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 30 MAY 2006

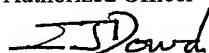
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Applicant's or agent's file reference 654008C:JFM:NXL	<b>FOR FURTHER ACTION</b>		See Form PCT/IPEA/416
International application No. <b>PCT/AU2004/001570</b>	International filing date ( <i>day/month/year</i> ) 12 November 2004	Priority date ( <i>day/month/year</i> ) 13 November 2003	
International Patent Classification (IPC) or national classification and IPC  Int. Cl.  See separate sheet			
Applicant UNIVERSITY OF SYDNEY, THE et al			

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 6 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
  - ☒ (*sent to the applicant and to the International Bureau*) a total of 19 sheets, as follows:
    - ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
    - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
  - ☐ (*sent to the International Bureau only*) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
- This report contains indications relating to the following items:
 

<input checked="" type="checkbox"/> Box No. I	Basis of the report
<input type="checkbox"/> Box No. II	Priority
<input checked="" type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/> Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/> Box No. VI	Certain documents cited
<input type="checkbox"/> Box No. VII	Certain defects in the international application
<input checked="" type="checkbox"/> Box No. VIII	Certain observations on the international application

Date of submission of the demand 13 September 2005	Date of completion of this report 01 March 2006
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer  <b>IAN DOWD</b> Telephone No. (02) 6283 2273

## Box No. I

## Basis of the report

1. With regard to the language, this report is based on:

☒ The international application in the language in which it was filed

☐ A translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3(a) and 23.1 (b))

☐ publication of the international application (under Rule 12.4(a))

☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-71 as originally filed/furnished

pages\* received by this Authority on \_\_\_\_\_ with the letter of

pages\* received by this Authority on \_\_\_\_\_ with the letter of

☒ the claims:

pages as originally filed/furnished

pages\* as amended (together with any statement) under Article 19

pages\* 72-87 received by this Authority on 13 September 2005 with the letter dated the same

pages\* 88-90 received by this Authority on 13 February 2006 with the letter dated the same

☒ the drawings:

pages 1-7 as originally filed/furnished

pages\* received by this Authority on \_\_\_\_\_ with the letter of

pages\* received by this Authority on \_\_\_\_\_ with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/figs

☐ the sequence listing (*specify*):

☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/figs

☐ the sequence listing (*specify*):

☐ any table(s) related to the sequence listing (*specify*):

\* If item 4 applies, some or all of those sheets may be marked "superseded."

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: 1-19 (all in part)

because:

☐ the said international application, or the said claims Nos.

relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-19 (all in part) are so unclear that no meaningful opinion could be formed (*specify*):

The claims are extremely broad in scope and encompass a vast number of possible compounds. A complete search of the claims was therefore not feasible. Consequently this written report is based only on quaternary ammonium and quaternary phosphonium compounds in so far as covered by the search.

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*)

☐ no international search report has been established for said claim Nos.

☐ A meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ Furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ Furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ Pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ A meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims 1-19	YES
	Claims	NO
Inventive step (IS)	Claims 1-19	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-19	YES
	Claims	NO

**2. Citations and explanations (Rule 70.7)**

The following documents were identified in the International Search Report:

- D1 Antimicrobial Agents & Chemotherapy (2004), 48(5), 1561-1569
- D2 J. Med. Chem. (1997), 40, 3557-3566
- D3 Antimicrobial Agents & Chem. (2003), 47(8), 2598-2605
- D4 Antimicrobial Agents & Chem. (2003), 47(8), 2590-2597
- D5 WO 1998/004252
- D6 EP 494 613
- D7 JP 2000-313171
- D8 Chemical Abstract 126:180319
- D9 Chemical Abstract 129:294300
- D10 Chemical Abstract 132:116550
- D11 Chemical Abstract 91:101848
- D12 Chemical Abstract 130:38597
- D13 Chemical Abstract 132:231503

D1 was published prior to the international filing date of the present application, but later than the priority date claimed. Under PCT guidelines, this document is excluded from consideration during international preliminary examination. However, D1 is nevertheless included here for the purpose of information. This is based on the assumption that the claimed priority date is valid. If this date is subsequently found invalid, then D1 may become relevant during national examination.

D2-D5 all disclose quaternary ammonium or quaternary phosphonium compounds that are used in the treatment of malaria. The claims as amended now exclude compounds encompassed by the present formula (I) Consequently claims 1-19 are novel in view of these documents.

(see also supplemental box)

**Box No. VIII**    **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claims 1-19 are not fully supported by the description. As previously indicated, the claims are extremely broad in scope and encompass a vast number of possible compounds. However the description only provides support for a limited number of quaternary ammonium and quaternary phosphonium derivatives. Furthermore, the proviso associated with claim 1 excludes over 160 substances, which is several times larger than the number of preparative examples given in the specification.

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of: International Patent Classification (IPC)

*C07C 211/63* (2006.01) *A61P 31/12* (2006.01) *C07D 233/64* (2006.01)  
*A61K 31/14* (2006.01) *A61P 33/00* (2006.01) *C07D 295/037* (2006.01)  
*A61K 31/66* (2006.01) *C07C 237/08* (2006.01) *C07D 453/02* (2006.01)  
*A61P 31/04* (2006.01) *C07D 213/04* (2006.01) *C07F 9/54* (2006.01)

Action date: 1 March 2006

Continuation of: Box No. V

D6-D12 also disclose quaternary ammonium or quaternary phosphonium derivatives. These compounds have also been excluded from the scope of the claims and hence claims 1-7 are considered novel in light of this prior art.

D13 discloses the use of quaternary ammonium compounds for the treatment of malaria. These compounds have also been excluded from the scope of the claims. Claims 9-11 therefore are considered novel in view of this document.

None of D2-D17 describes the use of quaternary ammonium or quaternary phosphonium compounds for the treatment of fungal or bacterial infections, or for the inhibition of phospholipase enzymes. Consequently claims 12-19 are novel and inventive.

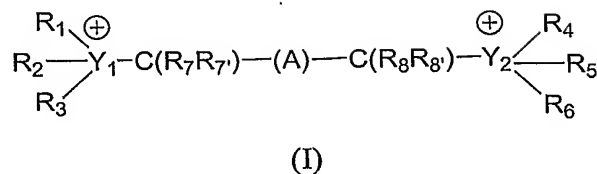
With regard to inventive step, the problem to be overcome is to provide improved anti bacterial or anti fungal agents. The application addresses this need by providing bis-cationic quaternary ammonium and/or quaternary phosphonium compounds. None of the documents cited as prior art would lead the person skilled in the art to use quaternary ammonium or quaternary phosphonium derivatives for the treatment of bacterial or fungal infections. An inventive step therefore can be acknowledged.

**Industrial Applicability**

Claims 1-19 meet the requirements for industrial applicability.

**CLAIMS:**

1. A compound of Formula (I)



5 wherein:

- (1)  $\text{Y}_1$  and  $\text{Y}_2$  may be the same or different and are independently selected from N and P;

$\text{R}_1$  to  $\text{R}_6$  may be the same or different and are independently selected from the group consisting of optionally substituted  $\text{C}_{1-10}$  alkyl, optionally substituted  $\text{C}_{2-10}$  alkenyl, optionally substituted  $\text{C}_{2-10}$  alkynyl, optionally substituted  $\text{C}_{3-10}$  cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl, hydroxyl, halogen,  $\text{O}(\text{C}_{1-6}$  alkyl),  $\text{C}(\text{O})\text{O}(\text{C}_{1-6}$  alkyl),  $\text{OC}(\text{O})(\text{C}_{1-6}$  alkyl),  $\text{NO}_2$ , amino, hydroxy $\text{C}_{1-6}$  alkyl, aryl,  $\text{OC}(\text{O})\text{Ph}$ , and  $=\text{C}(\text{Ph})_2$ ; or

$\text{R}_1$  and  $\text{R}_2$  together with the  $\text{Y}_1$  group to which they are attached, or  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  together with the  $\text{Y}_1$  group to which they are attached may optionally form a heterocycloalkyl group; and  $\text{R}_4$  and  $\text{R}_5$  together with the  $\text{Y}_2$  group to which they are attached, or  $\text{R}_4$ ,  $\text{R}_5$  and  $\text{R}_6$  together with the  $\text{Y}_2$  group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl, hydroxyl, halogen,  $\text{O}(\text{C}_{1-6}$  alkyl),  $\text{C}(\text{O})\text{O}(\text{C}_{1-6}$  alkyl),  $\text{OC}(\text{O})(\text{C}_{1-6}$  alkyl),  $\text{NO}_2$ , amino, hydroxy  $\text{C}_{1-6}$  alkyl, aryl,  $\text{OC}(\text{O})\text{Ph}$ , and  $=\text{C}(\text{Ph})_2$ ;

$\text{R}_7$ ,  $\text{R}_{7'}$ ,  $\text{R}_8$  and  $\text{R}_{8'}$  may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted  $\text{C}_{5-7}$  cycloalkyl, and  $-\text{C}(\text{O})-$ , wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl, hydroxyl, halogen,  $\text{NO}_2$ ,  $\text{C}(\text{O})\text{R}_{10}$ ,  $\text{OR}_{11}$ ,  $\text{CH}_2\text{OR}_{11}$ ,  $\text{CH}_2\text{NR}_{12}\text{R}_{13}$ ,  $\text{SR}_{11}$ ,  $\text{NR}_{12}\text{R}_{13}$ ,  $\text{CONR}_{12}\text{R}_{13}$ , amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

$\text{R}_{10}$  is selected from OH,  $\text{OR}_{11}$ ,  $\text{C}_{1-6}$  alkyl;

$R_{11}$  is selected from the group consisting of hydrogen, optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl and halogen;

$R_{12}$  and  $R_{13}$  are independently selected from the group consisting of hydrogen, optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl, halogen, amino, and  $C(O)OR_{11}$ ; or

$R_{12}$  and  $R_{13}$ , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl, halogen, amino, and  $C(O)OR_{11}$ ;

and when  $Y_1 = Y_2 = N$ , A comprises one or more groups selected from substituted alkylene, substituted alkenylene, substituted alkynylene, substituted phenyl, substituted  $C_{5-7}$  cycloalkyl, and  $-C(O)-$ , wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from  $C_4-C_6$  alkyl,  $C_{4-6}$  alkenyl,  $C_{4-6}$  alkynyl, hydroxyl, halogen,  $NO_2$ ,  $C(O)R_{10}$ ,  $OR_{11}$ ,  $CH_2OR_{11}$ ,  $CH_2NR_{12}R_{13}$ ,  $SR_{11}$ ,  $NR_{12}R_{13}$ ,  $CONR_{12}R_{13}$ , amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

$R_{10}$  is selected from OH,  $OR_{11}$ ,  $C_{1-6}$  alkyl;

$R_{11}$  is selected from the group consisting of hydrogen, optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl and halogen;

$R_{12}$  and  $R_{13}$  are independently selected from the group consisting of hydrogen, optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl, halogen, amino, and  $C(O)OR_{11}$ ; or

$R_{12}$  and  $R_{13}$ , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl, halogen, amino, and  $C(O)OR_{11}$ ;

and when  $Y_1 = Y_2 = P$ , A comprises one or more groups selected from substituted alkylene, substituted alkenylene, substituted alkynylene, substituted phenyl, substituted



C<sub>5-7</sub> cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, NO<sub>2</sub>, C(O)R<sub>10</sub>, OR<sub>11</sub>, CH<sub>2</sub>OR<sub>11</sub>, CH<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, SR<sub>11</sub>, NR<sub>12</sub>R<sub>13</sub>, CONR<sub>12</sub>R<sub>13</sub>, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

5 R<sub>10</sub> is selected from OH, OR<sub>11</sub>, C<sub>1-6</sub> alkyl;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl  
10 and halogen;

R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are  
15 independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>;

and when A is -CH<sub>2</sub>-C(O)PhCH<sub>2</sub>CH<sub>2</sub>-Ph-C(O)-CH<sub>2</sub>-, and R<sub>1</sub> and R<sub>4</sub> are hydroxy  
20 substituted ethyl, then one of R<sub>2</sub>, R<sub>3</sub>, R<sub>5</sub> and R<sub>6</sub> is different;  
and salts thereof;

or:

25 (2) Y<sub>1</sub> and Y<sub>2</sub> may be the same or different and are independently selected from N and P;

R<sub>1</sub> to R<sub>6</sub> may be the same or different and are independently selected from the group consisting of optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally  
30 substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxyC<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>; or

R<sub>1</sub> and R<sub>2</sub> together with the Y<sub>1</sub> group to which they are attached, or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> together with the Y<sub>1</sub> group to which they are attached may optionally form a heterocycloalkyl group; and R<sub>4</sub> and R<sub>5</sub> together with the Y<sub>2</sub> group to which they are attached, or R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> together with the Y<sub>2</sub> group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxy C<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>;

R<sub>7</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>8</sub> may be the same or different and are independently selected from F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C<sub>5-7</sub> cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, NO<sub>2</sub>, C(O)R<sub>10</sub>, OR<sub>11</sub>, CH<sub>2</sub>OR<sub>11</sub>, CH<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, SR<sub>11</sub>, NR<sub>12</sub>R<sub>13</sub>, CONR<sub>12</sub>R<sub>13</sub>, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R<sub>10</sub> is selected from OH, OR<sub>11</sub>, C<sub>1-6</sub> alkyl;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl and halogen;

R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>;

and salts thereof,

or:

(3)  $Y_1$  and  $Y_2$  are both nitrogen;

$R_1$  to  $R_6$  may be the same or different and are independently selected from the group consisting of substituted  $C_{1-10}$  alkyl, substituted  $C_{2-10}$  alkenyl, substituted  $C_{2-10}$  alkynyl, substituted  $C_{3-10}$  cycloalkyl, substituted aryl, substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from  $C_{4-6}$  alkyl,  $C_{4-6}$  alkenyl,  $C_{4-6}$  alkynyl, hydroxyl,  $O(C_{1-6}$  alkyl),  $C(O)O(C_{1-6}$  alkyl),  $OC(O)(C_{1-6}$  alkyl),  $NO_2$ , amino, hydroxy $C_{1-6}$  alkyl, aryl,  $OC(O)Ph$ , and  $=C(Ph)_2$ ;

$R_7$ ,  $R_7$ ,  $R_8$  and  $R_8$  may be the same or different and are independently selected from hydrogen, F and Cl;

$R_1$  and  $R_2$  together with the  $Y_1$  group to which they are attached, or  $R_1$ ,  $R_2$  and  $R_3$  together with the  $Y_1$  group to which they are attached may optionally form a heterocycloalkyl group; and  $R_4$  and  $R_5$  together with the  $Y_2$  group to which they are attached, or  $R_4$ ,  $R_5$  and  $R_6$  together with the  $Y_2$  group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, hydroxyl, halogen,  $O(C_{1-6}$  alkyl),  $C(O)O(C_{1-6}$  alkyl),  $OC(O)(C_{1-6}$  alkyl),  $NO_2$ , amino, hydroxy  $C_{1-6}$  alkyl, aryl,  $OC(O)Ph$ , and  $=C(Ph)_2$ ;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted  $C_{5-7}$  cycloalkyl, and  $-C(O)-$ , wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, hydroxyl, halogen,  $NO_2$ ,  $C(O)R_{10}$ ,  $OR_{11}$ ,  $CH_2OR_{11}$ ,  $CH_2NR_{12}R_{13}$ ,  $SR_{11}$ ,  $NR_{12}R_{13}$ ,  $CONR_{12}R_{13}$ , amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

$R_{10}$  is selected from OH,  $OR_{11}$ ,  $C_{1-6}$  alkyl;

$R_{11}$  is selected from the group consisting of hydrogen, optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from  $C_{1-4}$  alkyl, hydroxyl and halogen;

$R_{12}$  and  $R_{13}$  are independently selected from the group consisting of hydrogen, optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted

aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>;

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 9, 10, 11 or 12 alkylene groups and when R<sub>1</sub>, R<sub>2</sub> and Y<sub>1</sub> form a heterocycloalkyl group and when R<sub>4</sub>, R<sub>5</sub> and Y<sub>2</sub> form a heterocycloalkyl group, then R<sub>3</sub> and R<sub>6</sub> are different; and

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 9, 10 or 12 alkylene groups and R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Y<sub>1</sub> form a bicyclic group, then R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Y<sub>1</sub> together are different to R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and Y<sub>2</sub> when taken together;

and salts thereof,

or:

(4) Y<sub>1</sub> and Y<sub>2</sub> are both nitrogen;

R<sub>1</sub> to R<sub>6</sub> may be the same or different and are independently selected from the group consisting of optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxyC<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>; or

R<sub>1</sub> and R<sub>2</sub> together with the Y<sub>1</sub> group to which they are attached, or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> together with the Y<sub>1</sub> group to which they are attached may optionally form a heterocycloalkyl group; and R<sub>4</sub> and R<sub>5</sub> together with the Y<sub>2</sub> group to which they are attached, or R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> together with the Y<sub>2</sub> group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxy C<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>;

R<sub>7</sub>, R<sub>7'</sub>, R<sub>8</sub> and R<sub>8'</sub> may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted

phenyl, optionally substituted C<sub>5-7</sub> cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, NO<sub>2</sub>, C(O)R<sub>10</sub>, OR<sub>11</sub>, CH<sub>2</sub>OR<sub>11</sub>, CH<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, SR<sub>11</sub>, NR<sub>12</sub>R<sub>13</sub>, CONR<sub>12</sub>R<sub>13</sub>, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R<sub>10</sub> is selected from OH, OR<sub>11</sub>, C<sub>1-6</sub> alkyl;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl and halogen;

R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>;

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 12 alkylene groups, one of R<sub>1</sub> to R<sub>6</sub> is different; and

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 10 alkylene groups and four of R<sub>1</sub> to R<sub>6</sub> are C<sub>1-3</sub> alkyl, the remaining two of R<sub>1</sub> to R<sub>6</sub> are different; and

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 9, 10, 11 or 12 alkylene groups and when R<sub>1</sub>, R<sub>2</sub> and Y<sub>1</sub> form a heterocycloalkyl group and when R<sub>4</sub>, R<sub>5</sub> and Y<sub>2</sub> form a heterocycloalkyl group, then R<sub>3</sub> and R<sub>6</sub> are different; and

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 9, 10 or 12 alkylene groups and R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Y<sub>1</sub> form a bicyclic group, then R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Y<sub>1</sub> together are different to R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and Y<sub>2</sub> when taken together;

and salts thereof

or:

(5) Y<sub>1</sub> and Y<sub>2</sub> are both nitrogen;

R<sub>1</sub> to R<sub>6</sub> may be the same or different and are independently selected from the group consisting of optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and  
5 optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C<sub>4-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxyC<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>; or

R<sub>1</sub> and R<sub>2</sub> together with the Y<sub>1</sub> group to which they are attached, or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>  
10 together with the Y<sub>1</sub> group to which they are attached may optionally form a heterocycloalkyl group; and R<sub>4</sub> and R<sub>5</sub> together with the Y<sub>2</sub> group to which they are attached, or R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> together with the Y<sub>2</sub> group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups is substituted with one or more groups selected from C<sub>4-6</sub> alkyl, C<sub>4-6</sub> alkenyl, C<sub>4-6</sub> alkynyl,  
15 hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxy C<sub>4-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>;

R<sub>7</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>8</sub> may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene,  
20 optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C<sub>5-7</sub> cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, NO<sub>2</sub>, C(O)R<sub>10</sub>, OR<sub>11</sub>, CH<sub>2</sub>OR<sub>11</sub>, CH<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, SR<sub>11</sub>, NR<sub>12</sub>R<sub>13</sub>, CONR<sub>12</sub>R<sub>13</sub>, amino acids, dipeptidyl, tripeptidyl,  
25 tetrapeptidyl and pentapeptidyl;

R<sub>10</sub> is selected from OH, OR<sub>11</sub>, C<sub>1-6</sub> alkyl;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl,  
30 wherein said optional substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl and halogen;

R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted

aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are  
5 independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>;

and salts thereof,

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 12 alkylene groups, one of R<sub>1</sub> to R<sub>6</sub> is different; and

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 10 alkylene groups and four of R<sub>1</sub> to R<sub>6</sub>  
10 are C<sub>1-3</sub> alkyl, the remaining two of R<sub>1</sub> to R<sub>6</sub> are different; and

wherein when -C(R<sub>7</sub>R<sub>7'</sub>)-(A)-(CR<sub>8</sub>R<sub>8'</sub>)- is 9, 10 or 12 alkylene groups and R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Y<sub>1</sub> form a bicyclic group, then R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Y<sub>1</sub> together are different to R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and Y<sub>2</sub> when taken together;

15 or:

(6) Y<sub>1</sub> and Y<sub>2</sub> are both P;

R<sub>1</sub> to R<sub>6</sub> may be the same or different and are independently selected from the group consisting of optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl,  
20 optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxyC<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and  
25 =C(Ph)<sub>2</sub>; wherein at least one of R<sub>1</sub> to R<sub>6</sub> is substituted; or

R<sub>1</sub> and R<sub>2</sub> together with the Y<sub>1</sub> group to which they are attached, or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> together with the Y<sub>1</sub> group to which they are attached may optionally form a heterocycloalkyl group; and R<sub>4</sub> and R<sub>5</sub> together with the Y<sub>2</sub> group to which they are attached, or R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> together with the Y<sub>2</sub> group to which they are attached may  
30 optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxy C<sub>1-6</sub> alkyl, aryl, OC(O)Ph, and =C(Ph)<sub>2</sub>;

R<sub>7</sub>, R<sub>7'</sub>, R<sub>8</sub> and R<sub>8'</sub> may be the same or different and are independently selected from  
35 hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C<sub>5-7</sub> cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, hydroxyl, halogen, NO<sub>2</sub>, C(O)R<sub>10</sub>, OR<sub>11</sub>, CH<sub>2</sub>OR<sub>11</sub>, CH<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, SR<sub>11</sub>, NR<sub>12</sub>R<sub>13</sub>, CONR<sub>12</sub>R<sub>13</sub>, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R<sub>10</sub> is selected from OH, OR<sub>11</sub>, C<sub>1-6</sub> alkyl;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl and halogen;

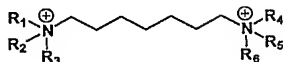
R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>;

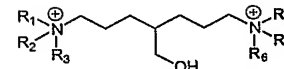
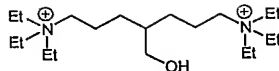
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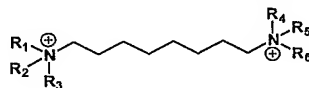
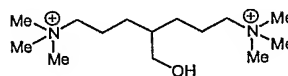
82



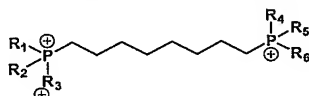
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Me, Et, allyl}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Me, } R_3 = R_6 = \text{Et, Pr}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Et, } R_3 = R_6 = \text{Me}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Pr, } R_3 = R_6 = \text{Me}$   
 $R_1 = R_2 = R_4 = R_5 = \text{allyl, } R_3 = R_6 = \text{Me}$



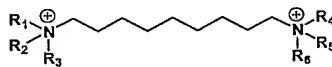
$R_1 = R_2 = R_4 = R_5 = \text{Me, } R_3 = R_6 = \text{Pr}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Pr, } R_3 = R_6 = \text{Me}$



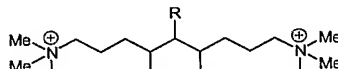
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Me, Et, Pr, Bu, pentyl, allyl}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Me, } R_3 = R_6 = \text{Pr, Bu, Decyl}$   
 $R_1 = R_4 = \text{Me, } R_2 = R_3 = R_5 = R_6 = \text{Hexyl, allyl}$   
 $R_1 = R_4 = \text{Me, } R_2 = R_5 = \text{Bu, } R_3 = R_6 = \text{octyl}$



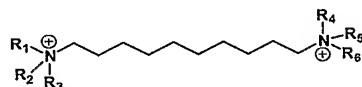
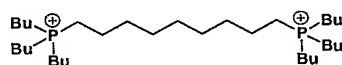
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{n-Bu, t-Bu, octyl}$



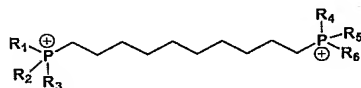
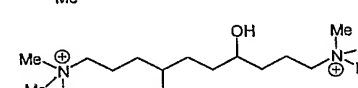
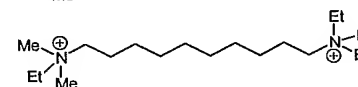
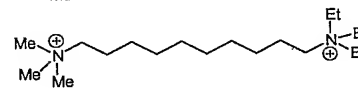
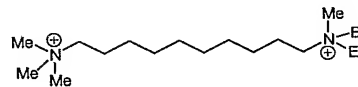
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Me, Et, allyl}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Me, } R_3 = R_6 = \text{Pr, pentyl}$   
 $R_1 = R_2 = R_4 = R_5 = \text{allyl, } R_3 = R_6 = \text{Et}$



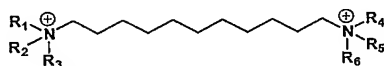
$R = \text{Pr, H, pentyl, hexyl, butyl, Me, Et}$



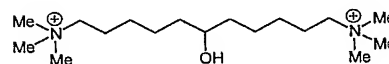
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Me, Pr, pentyl, butyl, allyl, ethyl, hexyl}$   
 $R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Bu, Et, hexyl, heptyl, pentyl, propyl, decyl, i-Pr, octyl}$   
 $R_1 = R_4 = \text{Me, } R_2 = R_3 = R_5 = R_6 = \text{allyl, ethyl}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Et, } R_3 = R_6 = \text{hexyl}$

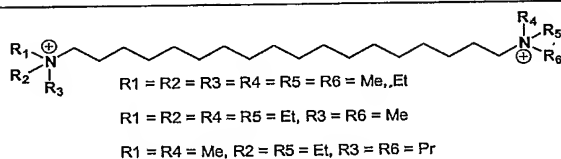
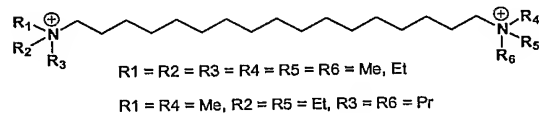
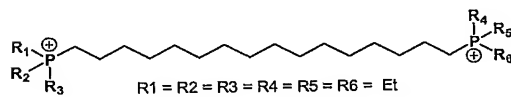
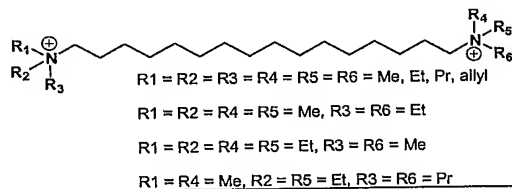
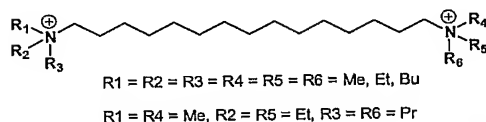
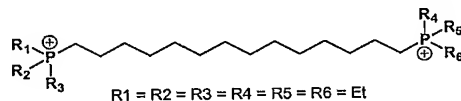
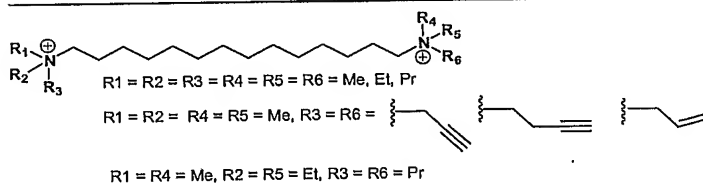
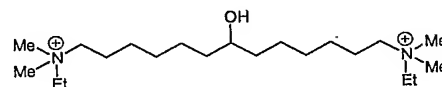
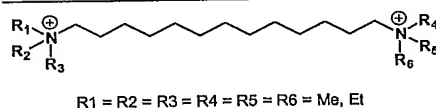
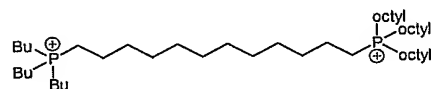
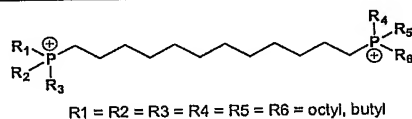
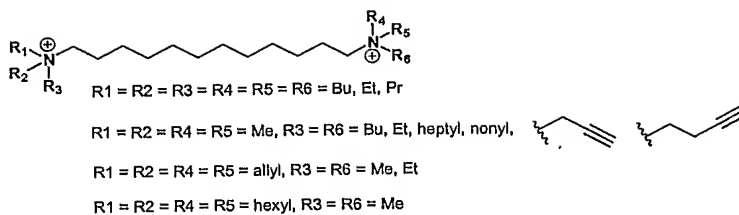


$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Me, Et, Bu, octyl}$

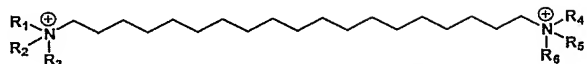


$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = \text{Me, Et}$   
 $R_1 = R_2 = R_4 = R_5 = \text{Me, } R_3 = R_6 = \text{pentyl}$

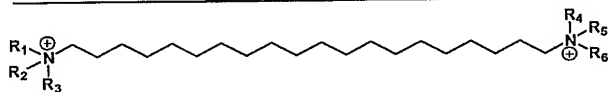




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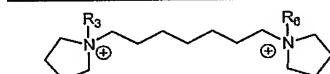
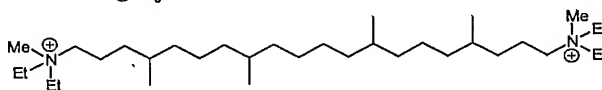


R1 = R2 = R3 = R4 = R5 = R6 = Me, Et

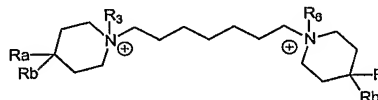
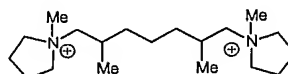


R1 = R2 = R3 = R4 = R5 = R6 = Me, Et, Pr

R1 = R4 = Me, R2 = R5 = Et, R3 = R6 = Pr

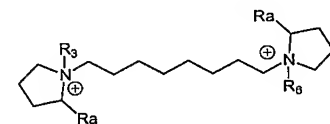
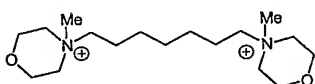


R3 = R6 = Me, Bu



R3 = R6 = Me; Ra, Rb = H

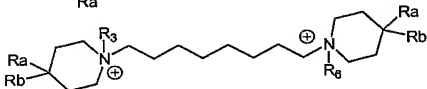
R3 = R6 = Me, Ra = Ph, Rb = CO<sub>2</sub>Et



R3 = R6 = Me, Ra = H

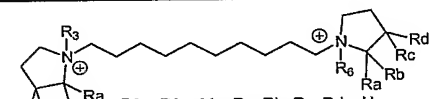
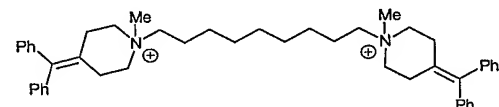
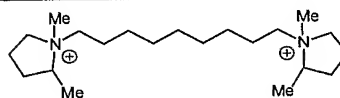
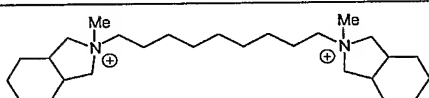
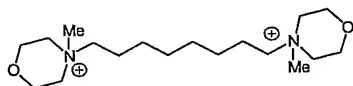
R3 = R6 = Me, Ra = Me

R3 = R6 = Me, Ra = Et



R3 = R6 = Me, Ra = Ph, Rb = CO<sub>2</sub>Et

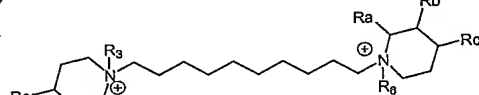
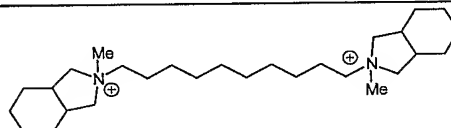
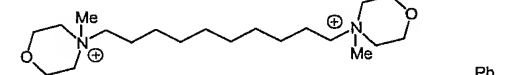
R3 = R6 = Me, Ra, Rb =  $\text{C}(\text{Ph})_2$



R3 = R6 = Me, Ra, Rb, Rc, Rd = H

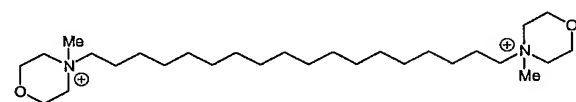
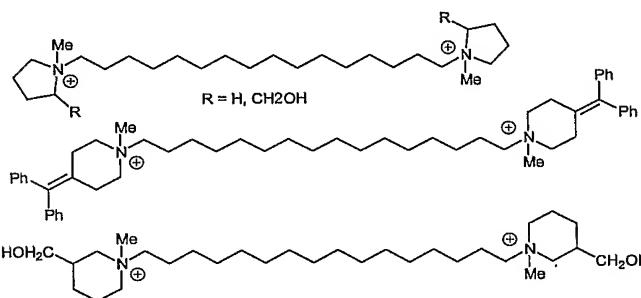
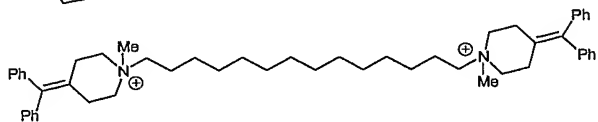
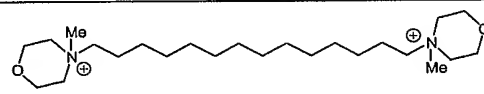
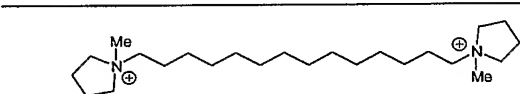
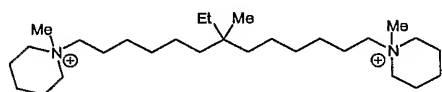
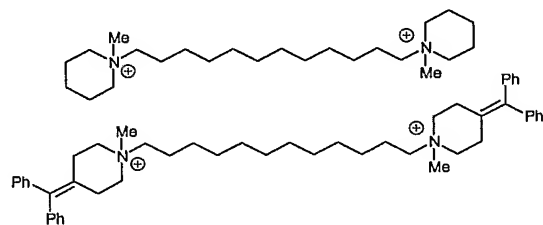
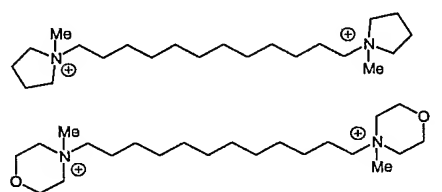
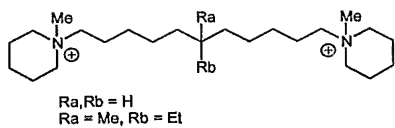
R3 = R6 = Me, Ra = Me, Rb, Rc, Rd = H

R3 = R6 = Me, Ra = Rb = Rc = Rd = Me



R3 = R6 = Me, Ra = Me, Rb = Rc = H  
R3 = R6 = Me, Ra = Et, Rb = Rc = H  
R3 = R6 = Et, Ra = H, Rb = OH, Rc = H  
R3 = R6 = Me, Ra = Rb = Rc = H  
R3 = R6 = Me, Ra = Rb = Rc = H  
R3 = R6 = Me, Ra = H, Rb = OC(=O)Pr, Rc = H  
R3 = R6 = Me, Ra = H, Rb = OAc, Rc = H  
R3 = R6 = Me, Ra = Rb = H, Rc = OC(O)Ph

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5

2. A compound according to claim 1, wherein  $Y_1$  and  $Y_2$  are each N.
3. A compound according to claim 1, wherein  $Y_1$  and  $Y_2$  are different.
4. A compound according to claim 1, wherein  $R_1$  to  $R_6$  are independently  
5 selected from the group consisting of optionally substituted  $C_{1-10}$  alkyl, optionally  
substituted  $C_{1-10}$  alkenylene, optionally substituted aryl, and optionally substituted  
heterocycloalkyl, or

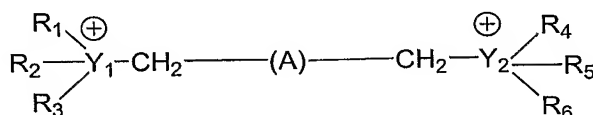
$R_1$  and  $R_2$  together with the  $Y_1$  group to which they are attached, or  $R_1$ ,  $R_2$  and  $R_3$   
together with the  $Y_1$  group to which they are attached form a heterocycloalkyl group; and  
10  $R_4$  and  $R_5$  together with the  $Y_2$  group to which they are attached, or  $R_4$ ,  $R_5$  and  $R_6$   
together with the  $Y_2$  group to which they are attached form a heterocycloalkyl group;

wherein said optional substituents are independently selected from  $C_{1-6}$  alkyl,  $C_{2-6}$   
alkenyl,  $C_{2-6}$  alkynyl, hydroxyl, halogen,  $O(C_{1-6}$  alkyl),  $C(O)O(C_{1-6}$  alkyl),  $OC(O)(C_{1-6}$   
alkyl),  $NO_2$ , amino, hydroxy  $C_{1-6}$  alkyl, and aryl.

5. A compound according to claim 1, wherein A comprises one or more groups  
selected from optionally substituted alkenylene, optionally substituted alkenylene,  
optionally substituted phenyl, and  $-C(O)-$ , wherein the substituents are independently  
selected from  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, hydroxyl, halogen,  $NO_2$ ,  $C(O)R_{10}$ ,  $OR_{11}$ ,  $CH_2OR_{11}$ ,  
 $CH_2NR_{12}R_{13}$ ,  $SR_{11}$ ,  $NR_{12}R_{13}$ ,  $CONR_{12}R_{13}$ , amino acids, dipeptidyl, tripeptidyl,  
15 tetrapeptidyl and pentapeptidyl.

6. A compound according to claim 1, wherein the length of A is from 5 to 9  
carbon atoms.

7. A compound according to claim 1, of Formula (Ia):



(Ia)

wherein

$Y_1$  and  $Y_2$  may be the same or different and are independently selected from N and  
P;

$R_1$  to  $R_6$  may be the same or different and are independently selected from the  
30 group consisting of optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl,  
optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally  
substituted aryl, optionally substituted heteroaryl, and optionally substituted  
heterocycloalkyl, wherein said substituents are independently selected from  $C_{1-6}$  alkyl,

C<sub>2-6</sub> alkenyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), NO<sub>2</sub>, amino, hydroxy C<sub>1-6</sub> alkyl, aryl, and OC(O)Ph; or

R<sub>1</sub> and R<sub>2</sub> together with the Y<sub>1</sub> group to which they are attached may optionally form a heterocycloalkyl group; and R<sub>4</sub> and R<sub>5</sub> together with the Y<sub>2</sub> group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, hydroxyl, halogen, O(C<sub>1-6</sub> alkyl), C(O)O(C<sub>1-6</sub> alkyl), amino, hydroxy C<sub>1-6</sub> alkyl, and aryl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, and optionally substituted phenyl, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, halogen, C(O)R<sub>10</sub>, OR<sub>11</sub>, SR<sub>11</sub>, CH<sub>2</sub>OR<sub>11</sub>, CH<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, NR<sub>12</sub>R<sub>13</sub>, CONR<sub>12</sub>R<sub>13</sub>, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R<sub>10</sub> is selected from OH, OR<sub>11</sub>, C<sub>1-6</sub> alkyl;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, and optionally substituted C<sub>3-10</sub> cycloalkyl, wherein said optional substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, aryl, and hydroxyl;

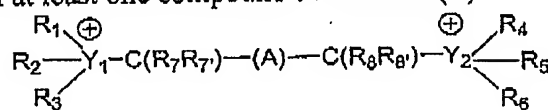
R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, aryl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>,

and salts thereof.

8. A compound according to claim 1, selected from 1,11-bis-(tributylammonium)undecane, 1,16-bis-(tributylammonium)hexadecane, 1,12-bis-(tripentylammonium)dodecane, 1,12-bis-(triethylammonium)dodecane, 1,12-bis-(trioctylammonium)dodecane, 1,12-bis-(triisobutylammonium)dodecane, 1,12-bis-(triisopentylammonium)dodecane, and 1,12-bis-(1-butylpyrrolidinium)dodecane, and salts thereof.

9. A method for one or more of treating, inhibiting, and preventing a bacterial or fungal infection in a vertebrate, said method comprising administering to said vertebrate an effective amount of at least one compound of Formula (II):



(II)

wherein

$Y_1$  and  $Y_2$  may be the same or different and are independently selected from N and P;

$R_1$  to  $R_6$  may be the same or different and are independently selected from the group consisting of optionally substituted  $C_{1-10}$  alkyl, optionally substituted  $C_{2-10}$  alkenyl, optionally substituted  $C_{2-10}$  alkynyl, optionally substituted  $C_{3-10}$  cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, hydroxyl, halogen,  $O(C_{1-6}$  alkyl),  $C(O)O(C_{1-6}$  alkyl),  $NO_2$ , amino, hydroxy  $C_{1-6}$  alkyl, aryl,  $OC(O)Ph$ , and  $=C(Ph)_2$ ; or

$R_1$  and  $R_2$  together with the  $Y_1$  group to which they are attached, or  $R_1$ ,  $R_2$  and  $R_3$  together with the  $Y_1$  group to which they are attached may optionally form an heterocycloalkyl group; and  $R_4$  and  $R_5$  together with the  $Y_2$  group to which they are attached, or  $R_4$ ,  $R_5$  and  $R_6$  together with the  $Y_2$  group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, hydroxyl, and halogen,  $O(C_{1-6}$  alkyl),  $C(O)O(C_{1-6}$  alkyl),  $NO_2$ , amino, hydroxy  $C_{1-6}$  alkyl, aryl, and  $=C(Ph)_2$ ;

$R_7$ ,  $R_{7'}$ ,  $R_8$  and  $R_{8'}$  may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted phenyl, optionally substituted  $C_{5-7}$  cycloalkyl, and  $-C(O)-$ , wherein the length of A is from 4 to 18 carbon atoms, wherein the substituents are independently selected from  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, hydroxyl, halogen, nitro,  $C(O)R_{10}$ ,  $OR_{11}$ ,  $CH_2OR_{11}$ ,  $CH_2NR_{12}R_{13}$ ,  $SR_{11}$ ,  $NR_{12}R_{13}$ ,  $CONR_{12}R_{13}$ , amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

$R_{10}$  is selected from OH,  $OR_{11}$ ,  $C_{1-6}$  alkyl, optionally substituted amino- $C_{1-6}$ -alkylsulfonate, optionally substituted amino- $C_{1-6}$ -alkylphosphonate, optionally substituted

amino-C<sub>1-6</sub>-alkyl-guanidiny], and optionally substituted amino-C<sub>1-6</sub>-alkyl-tri(C<sub>1-6</sub>-alkyl)ammonium;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted amino-C<sub>1-6</sub>-alkylsulfonate, optionally substituted amino-C<sub>1-6</sub>-alkylphosphonate, optionally substituted amino-C<sub>1-6</sub>-alkyl-guanidiny], and optionally substituted amino-C<sub>1-6</sub>-alkyl-tri(C<sub>1-6</sub>-alkyl)ammonium, wherein said optional substituents are independently selected from C<sub>1-4</sub> alkyl, hydroxyl and halogen

R<sub>12</sub> and R<sub>13</sub> are independently selected from the group consisting of hydrogen, optionally substituted C<sub>1-10</sub> alkyl, optionally substituted C<sub>2-10</sub> alkenyl, optionally substituted C<sub>2-10</sub> alkynyl, optionally substituted C<sub>3-10</sub> cycloalkyl, optionally substituted arylalkyl, optionally substituted alkylheteroaryl, optionally substituted amino-C<sub>1-6</sub>-alkylsulfonate, optionally substituted amino-C<sub>1-6</sub>-alkylphosphonate, optionally substituted amino-C<sub>1-6</sub>-alkyl-guanidiny], and optionally substituted amino-C<sub>1-6</sub>-alkyl-tri(C<sub>1-6</sub>-alkyl)ammonium, wherein said substituents are independently selected from C<sub>1-3</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>; or

R<sub>12</sub> and R<sub>13</sub>, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C<sub>1-3</sub> alkyl, hydroxyl, halogen, amino, and C(O)OR<sub>11</sub>.

10. The method according to claim 9, wherein said compound is a compound of Formula (I) as defined in claim 1.

11. The method according to claim 9, wherein the infection is a fungal infection.

12. The method according to claim 9, wherein the infection is a bacterial infection.

13. A method of inhibiting phospholipase in an organism comprising contacting said organism with an effective amount of at least one compound of Formula (I) or at least one compound of Formula (II).

14. The method according to claim 13, wherein the organism is selected from bacteria, fungi, virus, and parasite.

15. The method according to claim 13, wherein the phospholipase is Phospholipase B.

16. The method according to claim 13, wherein the organism is selected from the group consisting of: bacteria, fungi and virus.



17. A method for identifying an antimicrobial agent comprising contacting microbial cells with a compound of Formula (I) or Formula (II) suspected of having antimicrobial properties, determining whether said compound inhibits a microbial phospholipase enzyme, wherein inhibition of said phospholipase enzyme indicates antimicrobial activity, and thereby identifying an antimicrobial agent.

18. Use of a compound of formula (II) in the manufacture of a medicament for one or more of treating, inhibiting and preventing a bacterial or fungal infection in a vertebrate.

19. Use of at least one compound of formula (I), or at least one compound of formula (II), in the manufacture of a medicament for inhibiting phospholipase in an organism.

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